

## Beta-endorphin: The body's thermostat?

Four years ago, two proteins were identified as the brain's own natural pain-relieving molecules. Christened "enkephalins," after the Greek word for brain, these five-amino-acid proteins presaged an exciting era in pain research. And indeed, this era has arrived. But enkephalin research has opened a Pandora's box of discoveries, and neuroscientists are at a loss to explain them all.

Specifically, the enkephalins have turned out to be part of a 31-amino-acid protein called beta-endorphin, which is part of a larger, 91-amino-acid protein called beta-lipotropin, which in turn seems to come from a protein three times that size. What's more, when the enkephalins are extracted and used as drugs, they can do a variety of things: relieve pain, improve learning, reduce memory loss, induce pleasure and induce seizures. And while one preliminary trial suggested that injected beta-endorphin could help schizophrenics (SN: 9/17/77, p.182), another implied that an abnormal beta-endorphin in the blood might be a culprit in schizophrenia (SN: 7/8/78, p.29).

Now two more provocative findings about the endorphin clan have emerged. When endorphin action is blocked, schizophrenic hallucinations decrease (see following article). Beta-endorphin also appears to be involved in the body's regulation of heat, according to a report in the JUNE PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

Previous research has suggested that beta-endorphin helps the body adapt to heat. For instance, injections of low doses of the protein lead to a mild temperature elevation. The protein induces, in dogs, first the wet-dog shakes, presumably a heat-generating behavior, then copious salivation, a heat-loss behavior. Also, large doses of alkaloid opiates produce heat loss, and opiates and endorphins share some characteristics — they relieve pain, they act on the same nerve pain receptors and their action is reversed by naloxone. John W. Holaday of the Walter Reed Army Institute of Research in Washington, Eddie Wei of the University of California at Berkeley and Horace H. Loh and Choh Hao Li of the University of California at San Francisco have now carefully explored the possible involvement of the endorphin family in heat regulation.

First they exposed rats to acute or chronic heat. Half of the rats received injections of saline (and served as controls). The other half got injections of naloxone. The control rats adjusted to the heat after some time by lowering their body temperatures, but the rats that received naloxone did not, suggesting that naloxone was blocking the body's normal heat adaptation mechanism. But are the endorphins really the thermostat? The researchers

tested this possibility even more closely.

This time they removed the pituitary gland from some rats, because the pituitary is especially rich in endorphins and may be their actual source in the brain, but left the pituitary intact in other rats. Acute exposure to heat resulted in elevated temperatures in both groups of animals. Then both groups were given injections of naloxone. Naloxone increased the body temperature of the control rats even more, but not that of the animals without pituitaries, suggesting that the endorphins are most likely the endogenous heat thermostat that naloxone blocks.

These observations, the researchers conclude, "suggest that endorphins may function in adaptive mechanisms to heat." The researchers also suggest that the endorphins modulate both heat and pain sensations through the same neuroanatomical pathways. □

## Probing schizophrenia with naloxone

Insight into schizophrenia is coming from strange corners of medicine these days. A handful of scientists are treating schizophrenics with hemodialysis (SN: 7/8/78, p. 29). And now, behavioral researchers are probing the possible sources of hallucinations by injecting schizophrenic patients with the heroin antagonist naloxone.

Two years ago, scientists first detected abnormally high amounts of endorphins in the cerebrospinal fluid of acutely disturbed schizophrenic and manic patients. Since then, several other experiments have also implicated endorphins in schizophrenia, including studies where an unusual compound called leucine endorphin has been identified in the blood of schizophrenic patients who have undergone hemodialysis.

In a newly published study, researchers at Stanford University's Nancy Pritzker Laboratory of Behavioral Neurochemistry report that naloxone appears to alleviate symptoms — primarily auditory hallucinations — in a severely impaired subgroup of schizophrenics. The results indicate that naloxone blocks the action of endorphins by somehow altering various nerve receptor sites in the brain, according to Stanford's Stanley J. Watson.

"We think this has some theoretical significance" by indicating that the brain's natural "opiate system is involved in some psychosis," Watson told SCIENCE NEWS. But he adds that research in the field is still so preliminary that "we don't know quite how to interpret the findings ... we don't know exactly what's going on."

Watson concedes he may be a little

more cautious than usual because although this latest work corroborates a previous study, it conflicts with three other experiments that found essentially no effect of naloxone on auditory hallucinations. But he points out that those three studies used comparatively low doses of naloxone — about 10 times lower than those used in his study — and in some cases employed questionable methodology.

The Stanford group combed through about 1,000 general psychiatric patients before selecting nine that met their criteria. "We selected a rather rare group of patients ... clearly hallucinating," Watson notes. The subjects were rated before and after injections of naloxone or a placebo. (The two injections were separated by 48 hours and neither subjects nor experimenters were aware of which injection was the real thing.) The evaluations were based on a psychiatric rating scale and on self-reported instances of hallucinations.

Six of the nine patients showed "clear-cut improvement in hallucinations"; one showed borderline improvement; and two did not improve beyond the placebo effects, the researchers report in the July 7 SCIENCE. The research was not meant to test, nor do the results suggest, the clinical use of naloxone as a treatment for hallucinating schizophrenics. "Clinically, it would be impractical as a treatment," Watson says. Naloxone, even in high doses, is a "very short-acting agent" — although two subjects reported improvements for up to one to two days, the others reported the return of hallucinations in three to six hours after the injection.

The Stanford researchers are not sure exactly which endorphins may be involved in the hallucinating process, says Watson. Those may eventually be pinpointed in future experiments, he suggests. □

## Taking the clone to court

An Oxford University biologist has filed a \$7 million libel suit against J. B. Lippincott Co., publisher of David M. Rorvik's book *In His Image, the Cloning of a Man* (SN: 3/18/78, p. 164). The scientist, J. D. Bromhall, also seeks a court declaration that the book is a fraud and a hoax. He says that Rorvik wrote him asking for information in May 1977, six months after the clone was supposedly born. Bromhall charges that quotes in the book taken from a research paper abstract that he sent Rorvik create the impression that Bromhall was vouching for the book's accuracy. Bromhall claims that his reputation as an embryologist has been damaged. Lippincott attorney Peter Hearn told SCIENCE NEWS that the publishing company is aware of the suit, but so far has no response because it has not yet been served with a copy of the complaint. □